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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/801,085	03/15/2004	Eifion Phillips	A1695-5P US	9462

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EXAMINER	
COPPINS, JANET L	
ART UNIT	**PAPER NUMBER**
1626	

DATE MAILED: 10/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/801,085	PHILLIPS ET AL.	
	Examiner	Art Unit	
	Janet L. Coppins	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-8 and 18* is/are allowed.

6)☒ Claim(s) *9,10,16,17 and 19* is/are rejected.

7)☒ Claim(s) *11-15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-19 pending in the instant application.

Response to Amendment

1. Receipt is acknowledged of Applicants' Amendment and Response, submitted July 18, 2006, which has been reviewed by the Examiner and entered of record in the file. Accordingly, claims 1-3 and 8 have been amended.

2. The Examiner notes the deletion of non-elected subject matter from the claims with appreciation. Therefore, claims 1-8 are directed to allowable compounds and compositions. Pursuant to the procedures set forth in MPEP § 821.04(B), claims 9-19, directed to the processes of making and using an allowable product, previously withdrawn from consideration as a result of a restriction requirement, are hereby rejoined and fully examined for patentability under 37 CFR 1.104.

Because all claims previously withdrawn from consideration under 37 CFR 1.142 have been rejoined, **the restriction requirement as set forth in the Office action mailed on January 10, 2006 is hereby withdrawn**. In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 9-17 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The nature of the invention

The nature of the invention is the treatment or prevention of certain disease conditions arising from the dysfunction in the neurotransmission of the nicotinic acetylcholine receptor.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic or preventive regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic and preventive effects of all diseases, whether or not the disease is affected by the dysfunction of the nAChR would be vital.

In addition, it is the state of the art that there is no known cure or prevention for neurodegenerative diseases, including Alzheimer's disease, furthermore, there are only four medications available in the United States available to temporarily slow the early stages of Alzheimer's disease. The current drugs for the treatment of Alzheimer's disease, ARICEPT®, EXELON®, REMINYL® and COGNEX®, treat early stages of Alzheimer's disease by delaying the breakdown of acetylcholine. MEMANTINE®, which blocks excess amounts of glutamate, treats late stage Alzheimer's disease.
(URL:http://www.cnn.com/2003/HEALTH/conditions/09/24/alzheimers.drug.ap/index.html).

Hence, in the absence of a showing of correlation between all the diseases claimed as capable of treatment by the binding of nAChR, and since the treatment or prevention of Alzheimer's disease is mediated by the breakdown of acetylcholine or the inhibition of excess amounts of glutamate, one of skill in the art is unable to fully predict possible results from the administration of the compound of the claims due to the unpredictability of the specific binding of the claimed compounds to the appropriate nAChR subtype.

The amount of direction or guidance present and

the presence or absence of working examples

The only direction and guidance present in the specification are the binding assays discussed on pages 23-24 of the specification. Applicants have only provided data for two test compounds, demonstrating their binding affinity to α4 nAChR and α7 nAChR. There is no correlation shown between the binding affinity to nAChR with the prevention of Alzheimer's disease, i.e. the specification is silent as to the claimed compounds' efficacy for treating any neurodegenerative diseases *in vivo*.

The breadth of the claims and the quantity of experimentation needed

The breadth of the claims is the treatment of all possible diseases of claims 9 and 10, including Alzheimer's disease. The quantity of experimentation needed is undue experimentation. Based on the unpredictable nature of the invention and the state of the prior art and the breadth of the claims, one of ordinary skill in the art would be burdened with undue "experimentation study" to determine whether the claimed compounds not only inhibit the activity of a chemokine, but have efficacy for treating Alzheimer's disease, of which there is no known cure.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and whether Alzheimer's disease would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of claim 1 for the treatment or prevention of any and all diseases, conditions, or disorders encompassed by the language of claims 9 and 10, as well as Alzheimer's in claim 16, and , "a method for treating or preventing a condition or disorder arising from dysfunction of nicotinic acetylcholine receptor neurotransmission," of claim 17. As a result necessitating one of skill to perform an exhaustive search for which diseases can be treated by which compounds of claim 1 in order to practice the claimed invention.

While the Examiner agrees that Applicants are enabled for treating certain diseases, conditions, or disorders, she maintains that Applicants have not provided sufficient data to enable the treatment of the full range of diseases, conditions, or disorders that are encompassed by the claim language, "... a disorder arising from dysfunction of nicotinic acetylcholine receptor neurotransmission" of claims 9 and 10, or Alzheimer's of claim 16 or "neurodegenerative conditions in which there is loss of cholinergic synapses" of claim 17. Applicants have not shown that the instant compounds are beneficial for treating all types of neurodegenerative disorders or conditions. In most instances, the etiological causes of neurodegenerative disorders are unknown. While symptomatic treatments are available for many neurodegenerative disorders, drugs to reduce or prevent the neuronal loss in patients have yet to be identified. The broadly claimed "neurodegenerative conditions" includes many disorders that are extremely difficult to treat and have no known cure, such as Alzheimer's, Parkinson's disease, Huntington's, Tourette's, all of which demonstrate a loss of cholinergic synapses. Currently there are no medications on the market that even slow the progress of these diseases. Applicants do not provide any examples for treating neurodegenerative conditions, which is not

sufficient evidence for treating *all* known neurodegenerative conditions, particularly given their complexity and unknown causes.

Thus, the specification fails to provide sufficient support of the broad use of the compounds for the treatment of all disorders encompassed by claims 9, and 10 as well as certain diseases within claims 16 and 17.

The remaining method of use claims 11-15 are objected to as being dependent on rejected base claims.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 19 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim is drawn in terms of a process of preparation, but fails to recite any method steps beyond, "mixing the ingredients. " Therefore it is unclear which ingredients are intended and in what manner they are mixed. Clarification is requested.

Conclusion

7. Claims 1-19 are pending in the application, claims 1-8 and 18 appear to be in condition for allowance, claims 11-15 are objected to, and claims 9, 10, 16, 17, and 19 are rejected.

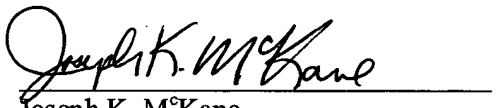
Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Coppins whose telephone number is 571.272.0680. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Joseph K. McKane can be reached on 571.272.0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Coppins
October 1, 2006



Joseph K. M°Kane
SPE, Art Unit 1626